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ASSESSMENT OF BONE DENSITY THROUGH CT SCAN IN ENUCLEATED ODONTOGENIC CYSTIC CAVITIES FILLED WITH PLATELET RICH FIBRIN AND ALLOPLASTIC BONE GRAFT

Dental Science

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ABSTRACT

BACKGROUND: Odontogenic cysts with large bony defects have always been the drawback for conservative management of these lesions. The healing of bony defects with bone regeneration of bone in cystic cavities has always been a challenging task. Various bone substitutes have been used to accelerate bone formation in cystic cavities. The greatest drawback of alloplasts is lack of osteogenic or osteoconductive property. This has led to a severe attempt to improve the physical properties of alloplastic materials by combining molecular, cellular and genetic tissue engineering technologies and one such attempt is platelet rich fibrin(PRF). The purpose of this study is to assess the healing of bone defects following cyst enucleation when osteoconductive alloplasts are combined with PRF.

MATERIALS AND METHODS: This single group randomized interventional study was done on 20 patients (14 male and 6 female) in the age group of 18 to 50 years. Patients with Mandibular or Maxillary odontogenic cysts with radiographic radiolucency measuring upto 5 cm in any of the three dimensions, and who were willing for a regular follow up were included. The enucleated cystic bony cavities were filled with autogenous PRF and alloplastic bone graft material. The patients were followed up for a period of two years. The bone formation in the cystic cavity was assessed preoperatively and post operatively using Orthopantomogram (OPG). The density of the bone formed post operatively was assessed using Computed Tomography (CT) scan after 6 months and was compared with the normal bone on the opposite side in Hounsefield units(HU). Infection and wound dehiscence were also assessed.

RESULTS AND CONCLUSIONS: The mean age group of the patients were 29.9 ± 8.15 years. 60% of the odontogenic cysts were found in the anterior region from canine to canine. Histopathologic diagnosis of treated cysts revealed 70% were radicular cysts and 30% were dentigerous cysts. The average dimensions of the cyst measured from the CT scan was: supero inferiorly 1.17 ± 0.41 cm, antero posteriorly 1.495 ± 0.86 cm, and medio lateral dimension 2.17 ± 0.75 cm. The average bone density in the cystic cavity filled with bone graft mixed with autogenous PRF achieved after six months was 374.35 ± 38.786 HU which was significantly higher than the average bone density on the contra lateral side (normal bone) which was 315.279 ± 43.476 HU.

KEYWORDS

Odontogenic cyst, Hydroxyapatite crystals, Platelet Rich Fibrin.

INTRODUCTION

Odontogenic cysts constitute 14-15% of Oral and Maxillofacial lesions. The management of odontogenic cysts have always been controversial.[1] The various treatment modalities for odontogenic cysts are enucleation, marsupialisation, enucleation with peripheral ostectomy, enucleation with chemical cauterization, segmental resection.[2] The factors which influence the treatment plan of an odontogenic cysts are age of the patient, location, extent of the lesion and histopathological features.[3] The treatment of odontogenic cysts should be individualized rather than a fixed treatment protocol. Large bony defects have always been the drawback of conservative management of these cysts. The healing of bony defects plays a prime role due to increased risk of pathological fracture of the weakened bone.[4]

Bone regeneration of cystic cavities has always been a challenging task to the oral and maxillofacial surgeons. Various bone grafts and bone substitutes have been used to accelerate bone formation in cystic cavities. Bone grafts can be osteogenic, osteoconductive or osteoinductive based on their mechanism to induce formation.[5] Based on the source they can be autogenous, allogenous, xenografts and alloplasts.[6] An osteogenic bone graft transfers osteocompetent cells to begin bone formation. The new bone at the site is formed from the cells transferred in the graft and not just from osteocompetent cells from defect site. Only autogenous bone grafts have osteogenic capacity.[7] Osteoinductive bone graft stimulates host mesenchymal cells to differentiate and begin bone formation by transfer of proteins which provide a signalling cascade from the host to form bone.[8] Osteoconductive bone grafts just provide a scaffold to create new bone. Bone healing can be primary and secondary. Secondary bone healing involves three major phases which include inflammation, repair and remodelling.

The various alloplastic materials used as bone substitutes are hydroxyapatite, tricalcium phosphate, biphasic calcium phosphate, calcium sulphate and biocompatible composite polymers. These synthetic bone grafts are osteoconductive materials. They resorb slowly and maintain space for bone formation and are available in block and particulate forms.[9] The greatest drawback of alloplasts is lack of osteogenic or osteoconductive property.[10] This has led to a

severe attempt to improve the physical properties of alloplastic bone grafts by combining molecular, cellular and genetic tissue engineering technologies. And one such attempt is platelet rich fibrin(PRF).

Platelet rich fibrin is a second generation platelet concentrate, first developed in France by Choukroun et al.[11] Fibrin is a support material for Bone Morphogenic Protein (BMP) transplant. After complete cyst enucleation the cavity is filled with blood clot. This blood clot is a physiologic version of PRF. This fibrin clot matrix acts as a trap for circulating stem cells. When the cystic cavity is filled with PRF, this physiologic healing phenomenon is accelerated. PRF being an organized fibrin matrix efficiently harnesses stem cells and thereby accelerates the healing process.[12]

The purpose of this paper is to assess the healing of bone defects following cyst enucleation when osteoconductive alloplasts are combined with PRF.

MATERIALS AND METHODS:

This single group randomized interventional study was carried out from April 2015 to April 2016 at Tamil Nadu Government Dental College and Hospital, Chennai, after obtaining clearance from the Institutional ethical committee. An informed consent was obtained from all patients. A total of 20 patients (14 male and 6 female) in the age group of 18 to 50 years were included in the study.

The inclusion criteria were Mandibular or maxillary odontogenic cysts with radiographic radiolucency measuring upto 5 cm in any of the three dimensions, and patients who were willing for a regular follow up.

Patients with infected odontogenic cysts, non odontogenic cysts, medically compromised patients, pediatric patients, patients with a history of recurrence, patients with bleeding and clotting disorders, patients on anti coagulant and anti platelet drugs were excluded from the study.

The patients were followed up for a period of two years. The bone formation in the cystic cavity was assessed preoperatively and post-operatively using Orthopantomogram (OPG). The density of the bone formed in the cystic cavity post operatively was assessed using Computed Tomography (CT) scan after 6 months and was compared with the normal bone on the opposite side quadrant in Hounsefield Units(HU). The other parameters assessed were presence of infection and wound dehiscence.

The following treatment protocol was followed in all patients. A thorough medical history was taken. After thorough clinical examination and OPG (Figure 1a,1b,1c), aspiration of cystic fluid was done in all cases. OPG was taken pre operatively and post operatively. Cone Beam Computed Tomography (CBCT) was taken preoperatively (Figure 2a,2b) and CT was taken post operatively to check for bone density using Hounsefield Units. An incisional biopsy was done in cases of large lesions >3 cm. In all cases, enucleation of the lesion was carried out. All patients were treated under strict aseptic conditions in Local or General Anesthesia depending on the size of the lesion and location.

Figure 1a: Pre operative Profile view
Figure 1b: Pre operative Intra oral view
Figure 1c: Pre operative OPG showing unilocular radiolucency in relation to 36 tooth

Figure 2a: Pre operative 3D CBCT
Figure 2b: Pre operative CBCT measurements of cystic cavity in axial view

A crevicular incision with one or two vertical releasing incisions were made, mucoperiosteal flap was raised, the cystic lining was identified and enucleated in toto (Figure 3a). The wound was irrigated with betadine and saline and the specimen was preserved for histopathologic evaluation.

Simultaneously PRF was prepared by withdrawing 10 ml of patient's own blood if the lesion was small. In case of large lesions, upto 30 ml of blood was withdrawn, and was collected in sterile glass tubes without anticoagulant and centrifuged for 10 mintues totally at 1000 RPM (revolutions per minute) for 1 minute and at 3000 RPM for 9 minutes using a table centrifuge. Three layers were formed in the sterile tube after centrifugation. The top layer consists of acellular plasma layer containing fibrinogen, the middle layer contains fibrin clot and the bottom layer red corpuscles. The middle layer is carefully separated using sterile scissors (Figure 3b,3c) and mixed with hydroxyapatite and β tricalcium phosphate bone crystals in a sterile cup (Figure 4a, 4b) and the mixture is carefully packed into the bony cavity where the cyst was enucleated (Figure 4c). The surgical site was primarily closed with 3-0 black silk. Suture removal was done after one week. The entire success of the technique depends on speed of blood collection and transfer to the centrifuge as the samples do not contain anticoagulant.

Figure 3a: Aspirated fluid and enucleated cystic lining
Figure 3b: Platelet Rich Fibrin (PRF) preparation after Centrifuge
Figure 3c: Obtaining PRF from three layers

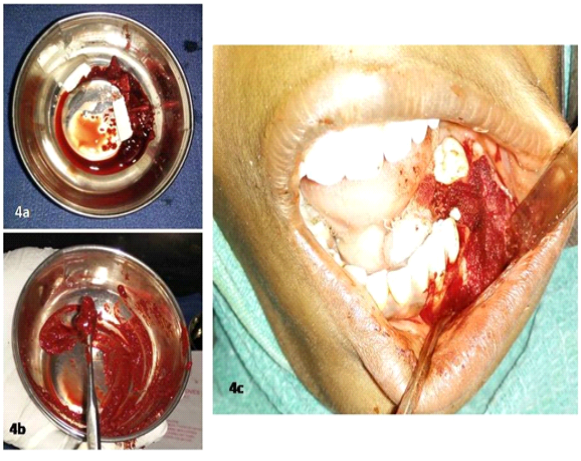

Figure 4a: PRF and Alloplastic bone graft material
Figure 4b: PRF mixed with Bone graft material
Figure 4c: Cystic cavity filled with mixture of Bone graft material and PRF

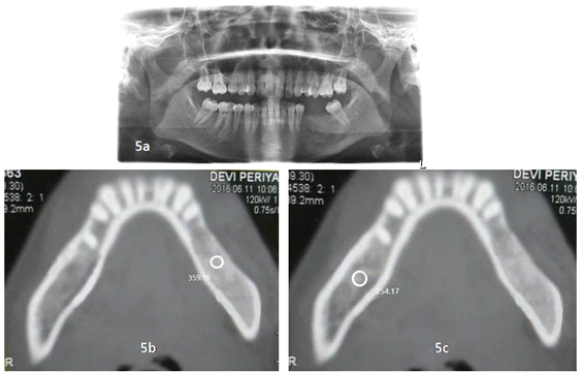

Figure 5a: Six months Post operative OPG
Figure 5b: Six months Post operative CT scan showing bone density in HU on surgical site
Figure 5c: Six months Post operative CT scan showing bone density in HU on contralateral side (normal bone)

OPG and CT scan were taken post operatively (Figure 5a, 5b, 5c) after a period of 6 months to assess the bone formation and the density of bone formed in the enucleated cavity site. Post operatively, wound dehiscence and presence of infection were evaluated clinically. All the patients were followed up for a period of two years.

RESULTS:

The study sample included 20 patients with a follow up period of two years. 70% were male patients. The mean age group of the patients were 29.9 ± 8.15 years. 60% of the odontogenic cysts were found in the anterior region from canine to canine. Histopathologic diagnosis of treated cysts revealed 70% were radicular cysts and 30% were dentigerous cysts. The average dimensions of the cyst measured from the CT scan was: supero inferiorly 1.17 ± 0.41 cm, antero posteriorly 1.495 ± 0.86 cm, and medio lateral dimension 2.17 ± 0.75 cm. Eighty percentage of the lesions were less than 3 cm which were treated by enucleation and in remaining 20% of cases where the greatest dimension was greater than 3 cm was treated with incisonal biopsy followed by enucleation. All the cystic cavities after enucleation was packed with bone graft mixed with autogenous platelet rich fibrin. There were no signs of infection, wound dehiscence, or paresthesia in any of the cases. Bone regeneration of the cystic cavity was assessed by CT scan where the bone density was measured in Hounsefield units after 6 months and was compared with contra lateral normal bone density (Figure 5b, 5c). The average bone density in the cystic cavity filled with bone graft mixed with autogenous PRF achieved after six months was 374.35 ± 38.786 HU which was significantly higher than the average bone density on the contra lateral side (normal bone) which was 315.279 ± 43.476 HU (Table 1).

Table 1: Demographic details and Clinical parameters

Sl No	Age	Sex	Site	Post op Histo-path diagnosis	Supero Inferior Dimension (cm)	Antero Posterior Dimension (cm)	Medio Lateral Dimension (cm)	Size Category	HU 6 months post op	HU non operated site
1	22	Female	Posterior	Dentigerous	0.5	2.4	1.4	< 3cm	315.37	287.58
2	18	Female	Posterior	Radicular	2.3	2.7	1.8	< 3cm	359.16	254.17
3	21	Male	Anterior	Radicular	0.8	0.4	1.7	< 3cm	348.81	320.57
4	32	Female	Posterior	Radicular	1.2	1.9	1.8	< 3cm	314.91	237.59
5	20	Male	Anterior	Radicular	1.1	0.7	2.3	< 3cm	379.49	318.71
6	25	Male	Anterior	Dentigerous	1.4	0.9	2.8	< 3cm	412.47	347.13
7	40	Male	Anterior	Radicular	1.3	1.3	3.9	> 3cm	441.36	371.46
8	32	Male	Posterior	Radicular	1.3	1.7	1.9	< 3cm	398.18	325.93
9	37	Female	Posterior	Dentigerous	0.9	2.4	1.5	< 3cm	327.91	281.78
10	27	Female	Anterior	Dentigerous	1	0.8	3.1	> 3cm	391.42	332.78
11	25	Female	Anterior	Radicular	1.9	0.7	2.2	< 3cm	431.83	378.47
12	23	Male	Posterior	Radicular	0.8	3.7	1.2	> 3cm	342.96	298.19
13	48	Male	Anterior	Dentigerous	1.1	0.9	2.8	< 3cm	371.93	304.19
14	22	Male	Posterior	Radicular	0.9	2	1.4	< 3cm	345.17	279.11
15	33	Male	Anterior	Dentigerous	0.9	0.5	3.3	> 3cm	389.19	342.19
16	42	Male	Anterior	Radicular	1.4	1	2.1	< 3cm	371.39	318.68
17	37	Male	Anterior	Radicular	1.1	1.1	2.4	< 3cm	375.59	338.29
18	34	Male	Anterior	Radicular	1.5	1.2	1.9	< 3cm	423.49	372.47
19	29	Male	Anterior	Radicular	0.9	1.5	2.8	< 3cm	417.39	364.42
20	31	Male	Posterior	Radicular	1.1	2.1	1.1	< 3cm	328.98	231.87
MEAN	29.9				1.17	1.495	2.17		374.35	315.279
SD	8.15				0.41	0.86	0.75		38.786	43.476

DISCUSSION:

The presence of epithelial rests even after odontogenesis makes the jaws most prone for the development of cysts. The diagnosis of odontogenic cysts should always be based on the triad of clinical, radiographic and histopathological examination. The aggressive behaviour and the recurrent nature of some of the odontogenic cysts have made histopathological examination mandatory. In the present study, 70% were male patients. This is in accordance with study by Deepashri Kambalimath et al[13] where males showed discrete predominance (58%) and also with other studies where the frequencies ranged from 52.5 to 60%. On the contrary female predominance was found in Brazilian population[13].

The mean age of the patients reported by Deepashri Kambalimath et al[13] in their study was 33.2 years. In the current study also the mean age group of the patients were 29.9 ± 8.15 years. As per the anatomic location, 60% of the odontogenic cysts were found in the anterior region. However other studies have shown that odontogenic cysts affected the mandible particularly posterior region followed by anterior region of maxilla. A study conducted in Lithuania[13] reported a higher frequency of odontogenic cysts in the maxilla with a proportion of 1.5:1.

n the present study the most common odontogenic cysts were radicular cysts followed by dentigerous cysts. Similar results were observed in studies by Nakamura et al[14] who studied a total of 1234 odontogenic cyst lesions out of which 41.2% were radicular cysts. Other prevalence rates of radicular cysts were 52.3% by Shear[15], 65.1% by Daley et al[16] and 24% by Koseoglu et al[17].

Partsch[18] recommended that only cysts with a maximum diameter of 2 cm can be treated by enucleation. In the present study lesions even upto 3cm were treated by enucleation.

Enucleation of odontogenic cysts results in defects of various shapes and sizes. Small surgical defects heal spontaneously as the bone cavities are replenished with blood clots which act as a scaffold for new bone formation. However, in large defects a blood clot in the bone defect could lead to infection or hematoma.

Hren and Milijavec[19] reported that large osseous defects created after enucleation of large jaw cysts showed slower post operative spontaneous regeneration than small osseous defects. Their results showed that the final bone density formed after 12 months in small defects (20-30mm) was 97% while in large defects it was 84% compared with healthy neighbouring bone density. Hence there is always a controversy regarding the filling of the osseous defects with bone substitutes after enucleation of large cysts.

Literature suggests that the use of autogenous bone grafts or alloplastic grafts accelerate the healing process of defects there by reducing the risk of jaw fractures and shortening the recovery period.

The shortcomings of autogenous bone grafts such as prolonged surgical time taken for graft harvesting, donor site morbidity, graft resorption and insufficient amount to replenish large defects have made the surgeons to move towards alloplastic graft materials and xenografts. Khaled et al[20] in their study reported that bone density 3 and 6 months after cyst enucleation with lesions measuring 1.5 to 3 cm was higher in the group of patients whose osseous defects was filled with Agipore granules than in the control group where the bone defects were not filled.

Ettl et al[21] reported that filling of bone defects had no added advantage and simple enucleation followed with filling up of defect with blood clot alone was sufficient to generate bone.

Chiapasco et al[22] and Wagdargi et al[23] also suggested that spontaneous bone regeneration could occur in large mandibular cyst without any bone substitutes. Shokier et al[24] observed spontaneous healing without the use of bone grafts in 20 patients with mono cortical bone defects ranging from 2.5 to 6 cm. They assessed bone density formed at intervals of 6, 12, 24 months and reported that there was a gradual reduction in size of osseous defects with bone density increasing significantly in the first six months.

Wagdargi et al[23] reported a statistically significant increase in bone density 6 months after enucleation and primary closure of 16 odontogenic cysts.

Schmitz and Hollinger[25] divided bone defects based on the number of walls surrounding the defect. Defects with two missing walls were classified as non critical size defects and defects with only one wall missing as critical size defects. They suggested that non critical size defects heal spontaneously without the use of bone substitutes regardless of the size of the defect. However, critical defects require reconstruction. In a study performed in rabbits, it was observed that spontaneous healing of osseous defects was superior when the defect was unicortical and less than 8 mm and failed when defects were bicortical and greater than 8 mm.

Regeneration is defined as reproduction or reconstruction of lost or injured part which fully restores the architecture or function of the part. Alloplastic materials inspite of their advantages lack osteogenic activity as they have to be resorbed and then replaced by new osteogenic tissue. They are osteoinductive. Hence to increase osteogenic properties, in the present study it was planned to add PRF along with nanobone. PRF was first developed in France by Choukran et al[11] for specific use in Oral and Maxillofacial Surgery. This technique neither uses any anticoagulant or bovine thrombin or any other gelling agent. Similar technique for obtaining PRF was done in the current study. In vitro studies have proved PRF releases autologous growth factors such as TGF-β (Transforming Growth Factor Beta) which induces massive synthesis of matrix molecules such as collagen 1 and fibronectin either by osteoblasts or fibroblasts and PDGF(Platelet Derived Growth Factor) for 1 week and upto 28 days. The natural and slow polymerisation occurring during centrifugation process of PRF leads to the formation of homogenous three dimensional organisation of the fibrin network resulting in increased incorporation of circulatory cytokinin in the fibrin matrix.

Marx et al[26] observed that when the PRP (Platelet Rich Plasma) was added to the bone grafts in mandibular defects, the maturation rate was better than that of grafts without PRP. Wiltfang et al[27] told that there is 8 to 10% more bone formation when PRP was added to β tricalcium phosphate. Kim et al[28] combined PRF with β tricalcium phosphate and reported rapid bone formation, remodelling and calcification in the second week than the β tricalcium phosphate alone in rabbits.

In a study by Eldibany et al[29] on the effect of nanobone in combination with PRF on bone regeneration after enucleation of mandibular cysts reported 31% reduction of the surface area of bone defect on the sixth month and 51% size reduction on the ninth month post-operatively. There was an increase of 22.2 % of bone density on the sixth month and 50.8% of bone density by 9th month. In contrast, Pradel et al[7] observed an increase of bone density of 48% only after 12 months following enucleation without grafting.

Chiapasco et al[22] reported mean value reduction in size of the defect of 12.34% after 6 months and 43.46% after 12 months while increase in bone density 37% after 6 months and 48.27% after 12 months.

In the current study, the average bone density achieved in the cystic cavities filled with bone graft mixed with autogenous PRF was 374.35 ± 38.786 HU after six months which was much higher than the average bone density on the contra lateral side (normal bone) which was 315.279 ± 43.476 HU.

GĂśtz et al[30] and Harms et al[31] observed high osteo conductivity of nanocrystalline hydroxyapatite. They suggested that high osteoconductivity of nanocrystalline hydroxyapatite was due to the presence of silicate ions which seem to accelerate bone formation and remodelling at Bone-Hydroxyapatite interface, as well as induce angiogenesis and rapid osteogenesis and prevented complete degradation, and nanobone were completely and firmly embedded with newly formed bone.

Jayalakshmi et al[32] in their study on PRF and β tricalcium phosphate for augmentation of periapical defect resulted in significant, progressive, and predictable clinical and radiographic bone regeneration.

Shivashankar et al[33] reported a case of an inflammatory periapical lesion in which a combination of PRF, hydroxyapatite and PRF membrane was used. Radiographically it was seen that Hydroxyapatite crystals have been almost completely resorbed and replaced with new bone at the end of two years. They concluded that the use of PRF in conjunction with Hydroxyapatite crystals might have accelerated the resorption of the graft crystals and would have induced rapid rate of bone formation.

Pappalardo et al[34] in their study on the efficacy of PRP and highly purified bovine xenograft reported 48% of the defect filled in the first post operative month and 90% of the defect filled by 6 months. Histological and histomorphometric analysis showed a significant presence of bone tissues and vessels, with newly formed bone in contact with anorganic bone particles. The mean volume of initial bone was 68 ± 1.6% and mean percentage of initial bone was 48 ± 2.4%. The mean percentage of inorganic particles in tissues was 20 ± 1.2% of the total volume.

Bolukbasi et al[35] did a histologic and histomorphometric study on the use of PRF in combination with biphasic calcium phosphate (BCP) in the treatment of bone defects and concluded that there was an increase in bone formation with the addition of PRF to BCP in surgically created defects in sheep tibia.

CONCLUSION:

The results of the current study shows that the combined use of PRF and Hydroxyapatite resulted in accelerated bone formation. However only radiographic evaluation has been done in this study. Histological examination is needed to assess the nature of newly formed bone. Long term clinical trials, comparative studies with control group are needed to assess the bone repair and regeneration of defects with this emerging biomaterial.

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